Patterns of survival and recurrence after surgical treatment of early stage non–small cell lung carcinoma in the ACOSOG Z0030 (ALLIANCE) trial

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Objective: Surgical resection has been the mainstay of curative treatment of early stage lung cancer in selected patients. We evaluated survival and patterns of recurrence after surgical resection for early stage lung cancer from the American College of Surgeons Oncology Group Z0030/Alliance trial.

Methods: One thousand eighteen patients enrolled in the Z0030 trial were analyzed according to clinical T stage. Differences between groups were compared using the 2-sample rank test or χ^2 test. Log rank test and Cox proportional hazards regression were used to compare survival and recurrence. To compare patients who underwent open versus video-assisted thoracoscopic surgery (VATS) resections, propensity-score matched analysis was performed. Seven hundred fifty-two patients (66 undergoing VATS and 686 undergoing open surgery) were classified into 5 equal-sized propensity-score groups. Proportional hazards regression was used to compare these outcomes.

Results: There were 578 patients with cT1 tumors and 440 patients with cT2 tumors. Median follow-up was 6.7 years. Median overall survival was 9.1 years (stage T1) and 6.5 years (stage T2). Overall survival at 5 years was 72% (stage T1) and 55% (stage T2). Local recurrence-free survival at 5 years was 95% (stage T1) and 91% (stage T2) ($P = .015$). Among patients with stage T1 cancer, 4.2% (23 out of 542) had local recurrences, whereas 7.3% (30 out of 409) of those with stage T2 tumors had local failure. There was no difference in the development of new primary tumors between stage T1 and stage T2 groups. In the propensity-score matched analysis of VATS versus open lobectomy patients, there was no difference in overall survival, disease-free survival, and freedom from development of a new primary tumor.

Conclusions: Results of patients with resected early stage non–small cell carcinoma from a large-scale, multicenter trial serve as benchmarks against which to compare nonsurgical therapies for early stage lung cancer. Propensity-score matched analysis shows no difference in survival between patients undergoing VATS and open lobectomy. (J Thorac Cardiovasc Surg 2014;147:747-53)

Surgical resection has been the gold standard for curative treatment of early stage lung cancer in appropriately selected patients. However, over the past decade, new technologies for treating early stage non–small cell lung carcinoma (NSCLC) have emerged as alternatives for patients who may be poor or marginal operative candidates. Outcomes of surgical treatment are needed to serve as reference points against which to compare the outcomes of these nonsurgical therapies in early stage lung cancer.

We performed a secondary analysis of a large-scale multicenter, randomized trial to determine the long-term clinical outcomes of patients undergoing surgical treatment for early stage NSCLC. The American College of Surgeons Oncology Group (ACOSOG) Z0030 (Alliance) trial was a prospective, randomized, multi-institutional clinical trial that was designed to determine the effect on survival of lymph node sampling versus mediastinal lymph node dissection in patients undergoing complete resection of early stage NSCLC.[1] Once the primary endpoints of the study were reached, we secondarily analyzed the data to determine overall survival and patterns of recurrence. The advantages of this dataset include the rigor and uniformity with which the trial was conducted regarding eligibility criteria, staging procedures, data collection, and surgical techniques as well as the fact that these data were audited. The long-term results derived from this study serve as benchmark data against which to compare the results of more recent nonsurgical therapies for the treatment of early stage lung cancer.

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Abbreviations and Acronyms

ACOSOG = American College of Surgeons Oncology Group
NSCLC = non–small cell carcinoma
VATS = video-assisted thoracoscopic surgery

METHODS

Details of the study design, eligibility requirements, and the morbidity and mortality of patients enrolled in the ACOSOG Z0030 (Alliance) trial have been previously reported.[1,2] The protocol was approved by a central institutional review board in addition to the institutional review board at each participating institution. All patients provided written informed consent before trial enrollment. In summary, eligible patients were required to be older than age 18 years, to have an Eastern Cooperative Oncology Group performance status lower than 3, and a tissue diagnosis of NSCLC clinical stage T1 or T2, N0 or non-hilar N1, M0 before randomization. Eligible patients had to be candidates for resection by means of pneumonectomy, lobectomy, bilobectomy, or segmentectomy. The type of resection (video-assisted thoracoscopic surgery [VATS] vs open) was recorded in the dataset. Patients with N2 metastases were excluded from randomization.

There were 1023 eligible patients who were evaluated for the following long-term outcomes: local, locoregional, distant recurrence, disease-specific, and overall survival (5 were excluded because clinical stage was not reported in the database). Thus in this study we evaluated 1018 patients by clinical T classification: 578 patients with T1 tumors and 440 patients with T2 tumors. Based on the Z0030 dataset definitions, recurrence was defined as local if it occurred in the adjacent lung parenchyma, bronchial stump, or the hilum adjacent to the bronchial stump. It was defined as regional if it occurred in the hilum (separate from bronchial stump), mediastinum, chest wall, or ipsilateral pleura. Recurrence was defined as distant if it occurred in a separate lobe of ipsilateral lung, contralateral thorax, supraclavicular lymph nodes, or distant organ.

Statistical Methods

Differences between groups with regard to clinical and tumor characteristics were compared using the 2-sample rank test or χ^2 test as appropriate. Cumulative survival probabilities were estimated using the Kaplan-Meier method. The log rank test and Cox proportional hazards regression were used to compare survival and recurrence across groups.

As an additional analysis, we evaluated the Z0030 dataset based on propensity-score matching to compare patients who underwent open versus VATS anatomic lung resections.[3] Clinical and tumor characteristics were used to build a propensity score for choice of treatments. These variables included age, sex, histology, performance status, tumor location, and clinical T classification (T1 vs T2). Propensity scores were developed to estimate the adjusted risks of perioperative outcomes associated with the approach of treatment (VATS vs open). Logistic regression was used to estimate the probability of VATS versus open given the previously listed risk factors. Patients were classified into 7 groups based on their propensity scores. Two hundred eight thoracotomy patients had lower scores than the lowest score of any VATS patient treated (group 0); 4 open lobectomy patients had higher scores than the highest VATS patient treated (group 6). Patients from these 2 groups were omitted from further analysis.[3] The remaining 752 patients (66 in the VATS group and 686 in the open lobectomy group) were classified into 5 equal-sized propensity score groups (groups 1-5). Proportional hazards regression with 5 strata (propensity score groups 1-5) was used to compare long-term outcomes between patients undergoing VATS and those undergoing an open procedure.

TABLE 1. Characteristics of patients in the American College of Surgeons Oncology Group Z0030/Alliance trial by clinical classification (n = 1023)

Clinical classification	n	%
T stage		
cT1	578	57
cT2	440	43
Pathologic stage		
IA	423	41
IB	418	41
IIA	37	4
IIB	97	9
IIIA	26	3
IIIB	19	2

RESULTS

Overall Survival

There were 1018 patients who were evaluated by clinical T classification: 578 patients with T1 tumors and 440 patients with T2 tumors. The stratification by clinical T classification is shown in Table 1. Median follow-up was 6.7 years in the entire cohort. The median overall survival for patients with T1 tumors was 9.1 years, whereas that for those with T2 tumors was 6.5 years. Overall survival and disease-free survival for clinical T1 and T2 patients are shown in Table 2.

The 5-year overall survival was 72% for T1 patients and 55% for T2 patients ($P < .001$) (Figure 1). Disease-free survival at 5 years was 77% for patients with T1 tumors and 58% for those with T2 tumors ($P < .001$) (Figure 2).

Local and Locoregional Recurrence

The 5-year local recurrence-free survival for the T1 cohort was 95% and for T2 group 5-year local recurrence-free survival was 91% ($P = .015$).

The 5-year locoregional recurrence-free survival was 88% for T1 patients, 84% for T2 patients ($P = .044$). The 5-year distant disease-free survival for the T1 patients was 83% and for the T2 patients was 66% ($P < .001$) (Table 2).

Of 542 patients with T1 tumors assessed for recurrence, 4.2% had local recurrences and 17.3% had distant metastases. Among patients with T1 tumors who were reported to develop recurrent tumor (125 patients), 6% of total recurrences were local alone, whereas 75.2% of recurrences were distant in nature (Table 3).

Of 409 patients with T2 tumors assessed for recurrence, 7.3% had local recurrences and 30.8% had distant metastases. Among patients with T2 tumors who developed recurrent tumor (156 patients), 8% of total recurrences were purely local, whereas 80.8% of recurrences included distant metastases (Table 3).

TABLE 2. Long-term outcomes in patients with clinical stage T1 and T2 tumors

	T1 (n = 578)		T2 (n = 440)				
	Median	5-year survival (95% CI)	Median	5-year survival (95% CI)	HR	95% CI	*P*
Overall survival	9.1	72 (68-76)	6.5	55 (51-60)	1.64	1.36-1.99	<.001
Disease-free survival*	NA	77 (73-81)	NA	58 (53-64)	1.88	1.49-2.38	<.001
Local disease-free survival†	NA	95 (93-97)	NA	91 (88-94)	1.96	1.14-3.37	.015
Local/regional disease-free survival‡	NA	88 (85-91)	NA	84 (80-88)	1.46	1.01-2.11	.044
Distant disease-free survival§	NA	83 (79-86)	NA	66 (61-71)	1.99	1.53-2.61	<.001
New primary‖	9	83 (79-86)	NA	84 (80-87)	0.84	0.61-1.16	.29

HR, Hazard ratio; *CI*, confidence interval; *NA*, median survival not achieved. *Disease-free survival (n = 542 (125 events) in the T1 group and n = 409 (156 events) in the T2 group): deaths are censored. †Local disease-free survival (n = 542 [23 events] in the T1 group and n = 409 [30 events] in the T2 group): deaths and regional/distant recurrence are censored. ‡Local/regional disease-free survival (n = 542 [57 events] in the T1 group and n = 409 [56 events] in the T2 group): deaths and distant recurrence are censored. §Distant disease-free survival (n = 542 [94 events] in the T1 group and n = 409 [126 events] in the T2 group): deaths and local/regional recurrence are censored. ||New primary (n = 564 [101 events] in the T1 group and n = 432 [57 events] in the T2 group): deaths are censored.

New Primary Tumors

There was no significant difference in the numbers of patients who developed new primary tumors in comparing the T1 and T2 groups. At 5 years, 83% of patients with T1 tumors and 84% of those with T2 tumors remained free of new primary tumors ($P = .29$) (Table 2).

Propensity-Score Matched Analysis of VATS Versus Open Lobectomy Patients

An additional analysis was performed to evaluate VATS versus open lobectomy patients based on propensity-score matched groups of the Z0030 cohort. The patient demographics for this analysis are shown in Table 4. Median follow-up was 7 years for the VATS patients (n = 66) and 6.7 years for the open lobectomy patients (n = 686). Overall survival between the VATS and open lobectomy groups were similar. The median overall survival for the VATS group was not achieved, and the 5-year survival was 71.6% (95% confidence interval [CI], 61.3%-83.6%). The median overall survival for the open lobectomy group was 8.4 years, and the 5-year survival was 65.9% (95% CI, 62.3%-69.7%) ($P = .36$) (Figure 3).

There was no difference in disease-free survival between the 2 groups (Figure 4). There were 13 (20%) patients in the VATS group who had a recurrence and 193 (28%) patients in the open lobectomy group. Median disease-free survival was not achieved in either the VATS or open lobectomy groups. There was no difference in 5-year disease-free survival: 75.2% in the VATS group, and 69.2% in the open lobectomy group ($P = .55$) (Table 5). Locoregional recurrence-free survival was similar between the 2 groups. The 5-year locoregional disease-free survival was similar, 82.0% in the VATS group and 86.1% in the open lobectomy group ($P = .58$). Distant recurrence-free survival was also similar between the 2 groups. The 5-year distant

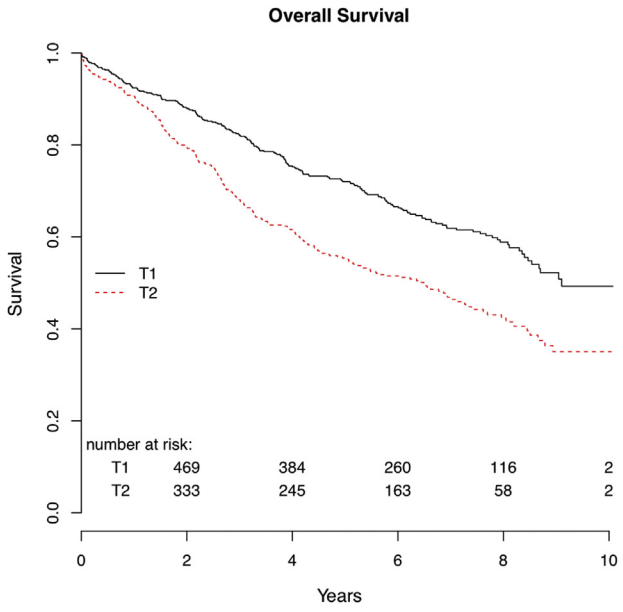

FIGURE 1. Overall survival, by cancer stage (T1 vs T2).

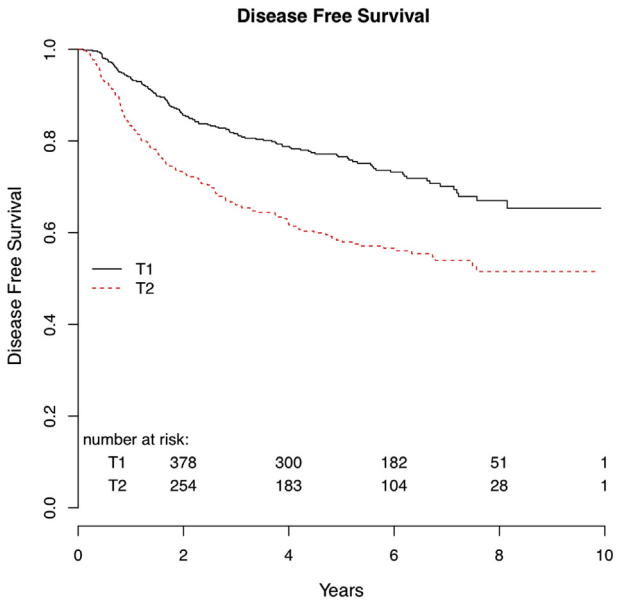

FIGURE 2. Disease-free survival, by cancer stage (T1 vs T2).

TABLE 3. Patterns of recurrences in the American College of Surgeons Oncology Group Alliance trial Z0030 data set, by clinical stage

	T1 (n = 542)	T2 (n = 409)
Local	7 (1)	13 (3)
Regional	22 (4)	13 (3)
Distant	68 (13)	99 (24)
Local/regional	2 (0.4)	3 (0.7)
Local/distant	10 (2)	9 (2)
Regional/distant	12 (2)	13 (3)
Local/regional/distant	4 (0.7)	5 (1)
Total No. of patients with recurrences	125	156*

Data are presented as n (%), unless otherwise indicated. *Location of recurrence was not indicated for 1 subject.

recurrence-free survival was 87.4% in the VATS group and 75.3% in the open lobectomy group ($P = .20$).

There was no statistical difference between the 2 groups in the time to development of a new primary tumor. The new primary tumor-free survival at 5 years was 87.8% in the VATS group and 81.7% in the open lobectomy group. There were 7 patients (11%) in the VATS group who had a new primary tumor, of which 4 were of lung origin. There were 118 patients (17%) in the open lobectomy group who had a new primary tumor, of which 34 were of lung origin.

DISCUSSION

To date the ACOSOG Z0030 (Alliance) trial is the largest prospective randomized trial of patients with early stage NSCLC undergoing surgical resection in the United States. Thus the outcomes of resected clinical T1 and T2 NSCLC reported in this study provide important points of reference with which to compare results of nonsurgical treatments, which are being more often considered as alternatives to surgery in both inoperable and operable patients. These therapies are difficult to compare due to lack of uniformity in staging, pathologic confirmation, patient selection, interpretations of post-treatment response, and nonstandard treatment protocols (eg, fractionation and dose prescription regarding stereotactic body radiation therapy). Additionally, the radiographic definition of successful local control in patients treated with nonsurgical ablation is broad, including partial response, stable disease, as well as complete response by either computed tomography or positron emission tomography/computed-tomography scan. For example, an important consideration in evaluation of stereotactic body radiation therapy outcomes is that local control often refers to the radiographic response in the tumor bed alone, whereas local control in the surgical literature includes failure in the ipsilateral lobe, hilum, and ipsilateral/contralateral mediastinum.

The Z0030 cohort included patients who were clinically staged as having stage I NSCLC, although ultimately it represented those who were N2 and hilar N1 node-negative on initial nodal sampling before being randomized into the trial. In spite of this, 18% were found to have a pathologic stage more advanced than stage I, with 13% harboring occult N1 disease and 2% with occult N2 disease. Recent studies evaluating patients with clinical stage I NSCLC who underwent surgical resection report 29% to 35% pathologic upstaging at surgery.[4,5] In the absence of pathologic staging, patients

TABLE 4. Patient demographics for patients included in the propensity-based analysis

	VATS (n = 66)	Open lobectomy (n = 686)	P*
Age, y	72.9 (70.9 ± 9.7)	68.6 (68.1 ± 8.8)	.011 (.38)
Sex			.15
Women	38 (57.6)	331 (48.3)	(.99)
Men	28 (42.4)	355 (51.8)	
Histology			.029
Squamous cell	10 (15.2)	206 (30.0)	(.99)
Adenocarcinoma	45 (68.2)	354 (51.6)	
Large cell	2 (3.0)	36 (5.3)	
Bronchoalveolar	8 (12.1)	57 (8.3)	
Other non–small cell carcinoma	1 (1.5)	33 (4.8)	
Performance status			.002
0	60 (90.9)	488 (71.1)	(.18)
1	5 (7.6)	192 (28.0)	
2	1 (1.5)	6 (0.9)	
Tumor location			.69
RUL	32 (48.5)	284 (41.4)	(.99)
RML	2 (3.0)	44 (6.4)	
RLL	8 (12.1)	112 (16.3)	
LUL	18 (27.3)	173 (25.2)	
LLL	7 (10.6)	85 (12.4)	
Clinical stage			.26
T1	44 (66.7)	408 (59.5)	(.89)
T2	22 (33.3)	278 (40.5)	
Pathologic T-stage			.78
T1	37 (56.1)	328 (48.0)	(.98)
T2	27 (40.9)	329 (48.2)	
T3	1 (1.5)	16 (2.3)	
T4	1 (1.5)	10 (1.5)	
Pathologic N-stage			.5
N0	61 (92.4)	592 (86.5)	(.65)
N1	5 (7.6)	81 (11.8)	
N2	0 (0)	11 (1.6)	
Pathologic stage			.54
IA	35 (53.0)	297 (43.5)	(.80)
IB	25 (37.9)	275 (40.3)	
IIA	2 (3.0)	28 (4.1)	
IIB	3 (4.6)	58 (8.5)	
IIIA	0 (0)	15 (2.2)	
IIIB	1 (1.5)	10 (1.5)	

Values are presented as n (%) or median (mean ± standard deviation). *VATS*, Video-assisted thoracic surgery; *RUL*, right upper lobe; *RML*, right middle lobe; *RLL*, right lower lobe; *LUL*, left upper lobe; *LLL*, left lower lobe. *χ^2 test for categorical variables and 2-sample *t* test (rank sum test) for continuous variables. *P* values in parentheses are Cochran-Mantel-Haenszel tests for categorical variables or linear models for continuous variables demonstrating that patient characteristics were similar across treatment groups after adjusting for propensity score groups.

TABLE 5. Long-term outcomes in propensity matched groups of patients undergoing video-assisted thoracic surgery (VATS) and open lobectomies

	VATS (n = 66)		Lobectomy (n = 686)				
	Median	5-year survival, % (95% CI)	Median	5-year survival, % (95% CI)	HR	95% CI	*P*
Overall survival	NA	71.6 (61.3-83.6)	8.4 y	65.9 (62.3-69.7)	1.22	0.8-1.87	.36
Disease-free survival*	NA	75.2 (63.5-89.1)	NA	69.2 (65.4-73.3)	1.19	0.67-2.10	.55
Local disease-free survival†	NA	88.0 (78.6-98.5)	NA	92.6 (90.2-95.0)	0.58	0.23-1.50	.26
Local/regional disease-free survival‡	NA	82.0 (71.5-94.1)	NA	86.1 (83.1-89.2)	0.81	0.39-1.70	.58
Distant disease-free survival§	NA	87.4 (77.6-98.4)	NA	75.3 (71.7-79.1)	1.65	0.77-3.55	.20
New primary‖	NA	87.8 (79.6-96.8)	9.0	81.7 (78.3-85.3)	1.71	0.79-3.72	.17

HR, Hazard ratio; *CI*, confidence interval; *NA*, median survival not achieved. *Disease-free survival (n = 47 in the VATS group and n = 652 in the lobectomy group). Deaths are censored. †Local disease-free survival (n = 47 in the VATS group and n = 652 in the lobectomy group). Deaths and regional/distant recurrence are censored. ‡Local/regional disease-free survival (n = 47 in the VATS group and n = 652 in the lobectomy group). Deaths and distant recurrence are censored. §Distant disease-free survival (n = 47 in the VATS group and n = 652 in the lobectomy group). Deaths and local/regional recurrence are censored. ‖New primary (n = 64 in the VATS group and n = 673 in the lobectomy group). Deaths are censored.

undergoing nonsurgical treatments are subject to clinical understaging. Yet studies of these latter treatments report low rates of local failure; for example, the Radiation Therapy Oncology Group 0236 trial (which enrolled patients with cT1-2N0 NSCLC for treatment by stereotactic body radiation therapy) reported a 3-year primary tumor control of 97.6% and local control of 90.6%.[6] One rationale behind such low rates of local failure may be that studies performed in patients deemed medically inoperable due to other comorbidities underrepresent actual rates of failure on account of censoring patients who die as a result of noncancer causes without documentation of recurrence.

Thus far, absence of long-term follow-up in studies involving nonsurgical treatments so far precludes formation of any guidelines for potentially operable candidates with early stage NSCLC. Long-term follow-up is required because local recurrence has been shown to occur at the site of primary tumor after an extended period following treatment (10 years).[7,8] Recent data from the completed Radiation Therapy Oncology Group 0618 trial, which evaluated operable patients undergoing stereotactic body radiation therapy for early stage NSCLC report local failure (primary tumor plus involved lobe failure) rates of 19.2% at 2 years.[9] In contrast, within the Z0030 cohort the local failure rate was 4% in the T1 patients and 7% in the T2 patients at a median follow-up of 6.7 years. Because the outcomes in our study evaluated the Z0030 cohort by clinical T1 and T2 classification (without regard to eventual pathologic stage), they represent important points of reference for comparison with outcomes of nonsurgical treatment in patients of similar early stage.

Our analysis of the Z0030 data shows that the long-term outcomes between patients who underwent VATS

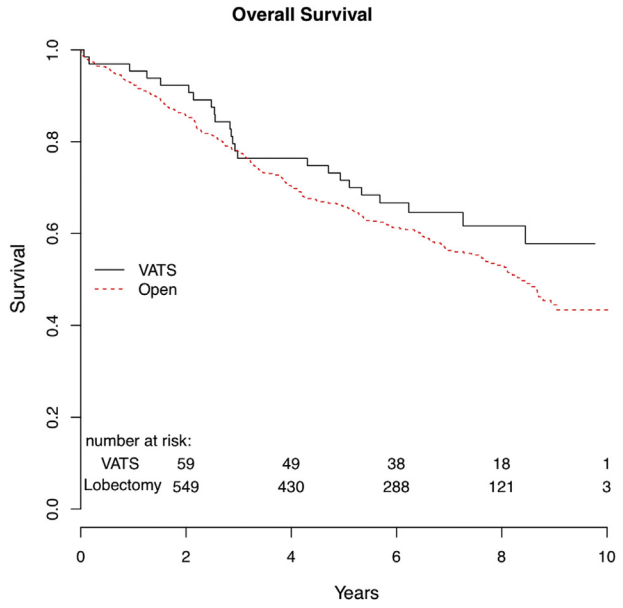

FIGURE 3. Overall survival, video-assisted thoracic surgery (*VATS*) versus open lobectomy.

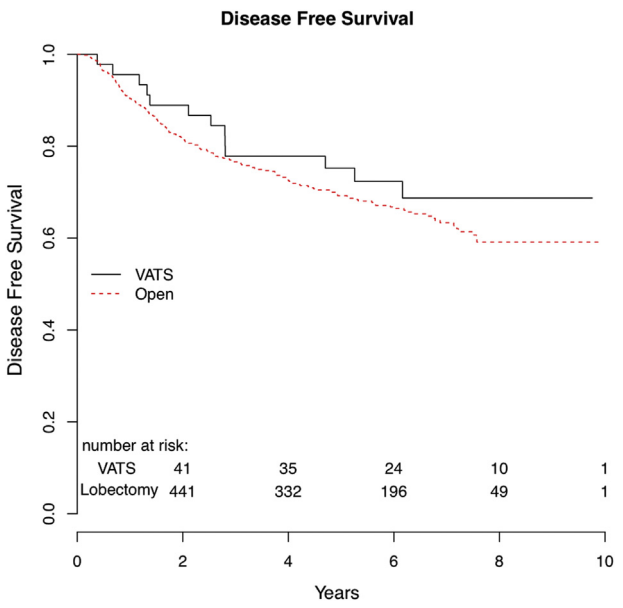

FIGURE 4. Disease-free survival, video-assisted thoracic surgery (*VATS*) versus open lobectomy.

lobectomy versus open lobectomy for early stage lung cancer are similar. There was no difference in overall survival, disease-free survival, or survival based on pattern of recurrence. There was no difference in time to locoregional recurrence between the VATS and open lobectomy groups. Based on the given data, the conclusion that VATS provides local control at least equivalent to that provided by thoracotomy is validated. Concern has been raised that VATS lobectomy for clinical T1-2 N0 NSCLC may lead to less complete N1 lymph node evaluation and lower rates of N1 upstaging compared with open lobectomy. Such detection of nodal involvement may extend the potential benefits of adjuvant chemotherapy to patients who otherwise would be offered none. The results of this study are unable to address this concern because the rate of pN1 involvement was low in both VATS and open lobectomy groups (8% and 12%, respectively; $P = .49$).

In the past, those who doubted the validity of the VATS lobectomy approach raised concerns that small lung lesions representative of synchronous primary tumors or metastatic disease may miss the opportunity for detection by bimanual palpation at the time of initial operation. This study shows that the numbers of patients who develop second primary tumors are not different between the VATS and open lobectomy approach. This finding is in agreement with the conclusions of a recent single-institution study that showed similar incidence of second primary tumors following lobectomy by VATS versus open technique.[10]

The limitations of this study include the fact that positron emission tomography/computed tomography was not required for entry into the trial; thus clinical staging by this means was not uniformly used. Data collected in follow-up was limited by return of data forms by the participating institutions. VATS sample size for the propensity-matched analysis was limited. At the time that the trial was conducted, adjuvant chemotherapy was not the standard of care for node-positive disease or tumors of size 4 cm or larger.[11] These nonetheless do not undermine the relevance of the reported outcomes in patients undergoing surgical resection with early stage NSCLC.

CONCLUSIONS

As nonsurgical treatments are more commonly used in treatment of early stage NSCLC, a critical evaluation of outcomes should be performed. The survival data and recurrence patterns following surgical treatment of clinical T1 and T2 lung cancers in the Z0030 cohort serve as benchmarks against which the outcomes of ablative techniques such as stereotactic body radiation therapy must be compared.

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Discussion

Dr Scott J. Swanson *(Boston, Mass).* Dr Su, that was an excellent presentation, and you showed extreme poise while you were waiting for your slides.

What is your message? Is it that we should pursue more minimally invasive strategies or their equivalent? I think I understand what you were getting at, but do you have a conclusion from what you presented here?

Dr Su. Thank you for your question and kind comments, Dr Swanson. There are several messages one can take from these data. The main one is that these data are issued from the largest randomized trial in the U.S. of surgical treatment for early-stage lung cancer. In terms of recurrence rates and survival, they represent a benchmark against which nonsurgical therapies (such as stereotactic body radiation therapy [SBRT] or radio-frequency ablation) must be compared. Additionally, these data provide continued support for the use of minimally invasive surgery as compared with open surgery in that recurrence rates, freedom from second primaries, and long-term survival of matched, early-stage lung cancer patients were similar regardless of surgical approach.

Dr Swanson. I have 1 further question. What do you make out of articles we have heard about recently about lymph node dissection or sampling or removal with video-assisted thoracoscopic surgery (VATS) versus open? It seems like your data show an

equivalent ability to get local and locoregional control. Is the correct conclusion that a VATS approach is equally good to getting local and regional control—meaning getting out lymph nodes—for early stage lung cancer? Am I understanding that correctly?

Dr Su. The VATS versus open lobectomy question is relevant because VATS has been suggested to have a lower risk profile, and the benefits of SBRT lie in its noninvasiveness and minimal risks. With regard to the lymph node dissection, only 7% of Z30 trial patients underwent VATS lobectomy. So these data are as good as it gets in terms of offering best outcomes, because most of the patients underwent open lobectomy.

Dr M. Blair Marshall *(Washington, DC).* I just have a comment. I would like to commend Stacey for taking this on. The stereotactic body radiation literature often compares results with old surgical results, not current data. It is important to continually update our results. There is too much variability in the literature and the definition of a local recurrence is variable in much of the stereotactic radiation literature. Those patients who are medically inoperable may never be sent for a biopsy of their recurrence. We have had no rigorous analysis of the data or outcomes in these studies. It is important to participate in these trials and have adequate follow-up of our patients. With the reports currently in the literature, and the very short-term outcomes being reported, radiation may seem like an equivalent alternative to surgery. However I am fairly certain that longer-term data will show that not to be the case.

Dr Raphael Bueno *(Boston, Mass).* Stacey, that was a great presentation.

Because you had a large number of patients and they are very much annotated, is it possible for you to look at those who are older, are the most frail, with the worst pulmonary function and additional comorbidities? Looking at the data for T1 is not going to make 90% much worse, but it will be potentially more comparable, and we can show that even in that population we do better. Is that something you can do?

Dr Su. Sure, that can be looked at. The Z30 trial was essentially looking at mediastinal nodal sampling versus dissection and the groups were randomized according to those criteria, but certainly that is something that can be looked into.

Dr David J. Sugarbaker *(Boston, Mass).* Very nice presentation, Dr Su. I have just a question about preoperative staging, particularly in the T2 lesions. Was there any systematic review as to which patients would have preoperative endobronchial ultrasound or mediastinoscopy?

Dr Su. The Z30 trial required patients to be nodenegative from the standpoint of N2 nodes and hilar N1 nodes. These patients were staged according to mediastinoscopy in addition to VATS and thoracotomy. Endobronchial ultrasound was not utilized during the time period of the study.

Dr Sugarbaker. How about positron emission tomography scans?

Dr Su. Positron emission tomography scans were not consistently used. The study was conducted before those scans were widely available.

Dr Bueno. But you looked at all T1s regardless of what the N status was to mimic what the SBRT people might be doing?

Dr Su. SBRT data is often quoted in terms of T1 and T2.

Dr Bueno. So some of your T1s were stage II, potentially?

Dr Su. These were pathologic T1 and pathologic T2 data.